VETERANS HEALTH ADMINISTRATION
OFFICE OF PATIENT CARE SERVICES
TECHNOLOGY ASSESSMENT PROGRAM

BRIEF OVERVIEW:

Systematic Reviews for Podiatry

Prepared by
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November 2009

A SUMMARY FOR HTA REPORTS
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This summary form is intended as an aid for those who want to record the extent to which an HTA report meets the 17 questions presented in the checklist. It is NOT intended as a scorecard to rate the standard of HTA reports – reports may be valid and useful without meeting all of the criteria that have been listed.

Brief Overview:
Systematic Reviews for Podiatry

November 2009

Item	Yes	Partly	No
Preliminary			
1. Appropriate contact details for further information?	√		
2. Authors identified?	√		
3. Statement regarding conflict of interest?	√		
4. Statement on whether report externally reviewed?		√	
5. Short summary in non-technical language?			√
Why?			
6. Reference to the question that is addressed and context of the assessment?	√		
7. Scope of the assessment specified?	√		
8. Description of the health technology?	√		
How?			
9. Details on sources of information?	√		
10. Information on selection of material for assessment?	√		
11. Information on basis for interpretation of selected data?	√		
What?			
12. Results of assessment clearly presented?	√		
13. Interpretation of assessment results included?	√		
What Then?			
14. Findings of the assessment discussed?	√		
15. Medico-legal implications considered?			√
16. Conclusions from assessment clearly stated?	√		
17. Suggestions for further actions?	√		

TECHNOLOGY ASSESSMENT PROGRAM

An Effective Resource for Evidence-based Managers

VA's Technology Assessment Program (TAP) is a national program within the Office of Patient Care Services dedicated to advancing evidence-based decision making in VA. TAP responds to the information needs of senior VA policy makers by carrying out systematic reviews of the medical literature on health care technologies to determine "what works" in health care. "Technologies" may be devices, drugs, procedures, and organizational and supportive systems used in health care. TAP reports can be used to support better resource management.

TAP has four categories of products directed toward filling urgent information needs of its VA clients. TAP assigns a category to each new request based largely on the availability of studies from results of initial searches of peer-reviewed literature databases:

- The ***Short report*** is a self-contained, rapidly-produced qualitative systematic review. It provides sufficient background information and clinical context to its subject to be accessible to a wide audience, including non-clinician managers.

- The ***Brief overview*** originated as an internal memo to VA clients with both well-defined and urgent information needs. It assumes sufficient existing knowledge regarding clinical context and technology issues by its readers to omit these components. It often requires some additional reading of documents (provided with the overview for the client) to obtain a full and comprehensive picture of the state of knowledge on the topic.
- The ***Outline and Bibliography*** provide structured support to client groups planning to conduct their own evidence reviews.

All TAP products are reviewed internally by TAP's physician advisor and key experts in VA. Additional comments and information on this report can be sent to:

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Elizabeth Adams Health System Specialist Boston	Consultation throughout project	Internal content and format review.
Elaine Alligood Information Specialist Boston	Literature database searches	Database searches: • Design/conduct technical strategy; • Choose/manage databases; • Strategy text and references for report. • TAP library/archive.
Bernard Spence Administrative Officer Boston	Administrative support	• Budget/resources; • "intelligent lay reader" review; • Project tracking.
Sarah Curran Library Technician Boston	Article retrieval	Information retrieval: • Full text from print journals and electronic resources; • Manage reference lists.
Valerie Lawrence Physician Advisor San Antonio	Content and methods review	Final review: • Internal consistency, • Clarity; • Clinical context; • Methods.

ABBREVIATIONS

AAI, ankle-arm (systolic pressure) index

ADFUS, Apligraf® diabetic foot ulcer study

AHRQ, Agency for Healthcare Quality and Research (US)

ANZHSN, Australia and New Zealand Horizon Scanning Network

ASERNIP-S, Australian Safety and Efficacy Register of New Interventional Procedures – Surgical

ATL, Achilles tendon lengthening

BSS, bioengineered skin substitute

CAI, chronic ankle instability

CCT, controlled clinical trial

CCOHTA, Canadian Coordinating Office for Health Technology Assessment

CI, 95% confidence interval

CRD, Centre for Reviews and Dissemination (York, UK)

CWH, complete wound healing

DASIDU, decision analysis for sampling and managing infected diabetic ulcers

DFU, diabetic foot ulcer

DMSO, di-methyl sulfoxide

DOR, diagnostic odds ratio

EP, end point

EVA, ethylene vinyl acetate

FU, follow up

GCSF, granulocyte colony stimulating factor

HBO, hyperbaric oxygen

ICSI, Institute for Clinical Systems Improvement (US)

In, indium

INAHTA, International Network of Agencies for Health Technology Assessment

ITT, intention to treat

JIA, juvenile idiopathic arthritis

LSE, living skin equivalent

MRI, magnetic resonance imaging

NHS, National Health Service (UK)

NIDDM, non insulin dependent diabetes mellitus

NNT, number needed to treat

NPV, negative predictive value

NPWT, negative pressure wound treatment

NS, not (statistically) significant

NSAID, non-steroidal anti-inflammatory drug

OR, odds ratio

OTC, over the counter or non-prescription

PDGF, platelet-derived growth factor

PDWHF, platelet-derived wound healing factor

PPP, palmoplantar pustulosis

PR, platelet releaseate

PUVA, psoralen ultraviolet A

QoL, quality of life

RA, rheumatoid arthritis

RBRVS, resource based relative value scale (US Medicare)

RCT, randomized controlled trial

Se, sensitivity

SC, standard care

Sp, specificity

TAP, Technology Assessment Program

Tc, technetium

TCC, total contact casting

TNP, topical negative pressure

VAC, vacuum-assisted closure

WBC , white blood cell

WCC, wound care center

WMD, weighted mean difference

BRIEF OVERVIEW:

Systematic Reviews for Podiatry

BACKGROUND

As support for national information letters, VHA's Podiatry Service asked TAP to review published literature, first on fungal toenail infection, and subsequently on basic foot care (nail care or callus debridement). TAP split its charge into two reviews: Toenail Onychomycosis and this one, which catalogs what is known from systematic reviews about the effectiveness of other interventions in foot care.

METHODS

Searches using "basic foot care " or terms for the procedures specified by Podiatry produced insufficient retrievals for review, so TAP approached its charge through a catalog of available systematic reviews, guidelines based on such reviews, and economic evaluations using high quality primary studies or reviews as sources of effectiveness data. This document will refer collectively to these synthesis publication types as "reviews".

As explained in greater detail below, reviews qualify as reproducible science. TAP identified available systematic reviews for any intervention relevant to Podiatry Service.

Selection criteria

Reviews were further required to be full-text available in English, to synthesize primary research in adult human subjects (or adults separately analyzed within a larger population), and to have been published or updated since 2000. Final updated searches were conducted on November 6, 2009.

TAP also included: technology assessments, guidelines, or economic evaluations clearly documenting sources of efficacy data and addressing interventions used in ambulatory podiatric primary care or for which primary care podiatrists are likely to refer patients. TAP included preliminary reviews (Cochrane protocols or horizon scanning summaries) as indicators of pending review availability. Podiatry Service reviewed a draft list of interventions to be covered and confirmed applicability to its needs.

Exclusion criteria

- Narrative reviews, opinion pieces, and other publications lacking primary clinical data;
- Reviews already included in other systematic reviews or independent queries to TAP;
- Cochrane protocols or other preliminary documents;
- Cost studies, i.e. evaluations of costs without comparative effectiveness data;
- "Quasi-systematic" reviews, i.e., those indexed or titled as systematic but which on close examination do not meet criteria or are inadequately reported to judge: quasi-systematic reviews may attend to some details of true systematic reviews but miss their essential spirit of critical analysis;
- Where reviews were conducted under industry support, we so indicate but do not exclude on industry support alone except in cases of payment for publication.

Analytic framework: Systematic reviews
Cook (1997) and Mulrow (1997) define systematic reviews:

> "*Systematic reviews are scientific investigations in themselves, with pre-planned methods and an assembly of original studies as their "subjects". They synthesize the results of multiple primary investigations by using strategies that limit bias and random error…"*

The same authors further specify characteristics of systematic reviews and contrast them with traditional narrative reviews, which synthesize an apparently unstructured array of articles without reporting methods of selection or quality assessment, and thus are prone to significant bias.

Systematic reviews:
- Ask a focused clinical question.
- Conduct a comprehensive search for relevant studies using an explicit search strategy.
- Uniformly apply criteria for inclusion and exclusion of studies.
- Rigorously and critically appraise included studies.
- Provide detailed analyses of the strengths and limitations of included studies.

Systematic reviews can be quantitative (i.e., meta-analytic, applying statistical methods to summarize study results) or qualitative; in either case the inferences or conclusions of the review must follow logically from the evidence presented. The rigor of this approach is illustrated by the place of systematic reviews in evidence grading schemes (Cook, 1995; Guyatt, 1995), where they receive the highest level designation. Cochrane reviews (www.cochrane.org), which set the standard for rigor of methods and validity of conclusions, are meta-analytic where primary studies permit.

The rigor of this approach is illustrated by the place of systematic reviews in evidence grading schemes (Cook, 1995; Guyatt 1995), where they receive the highest level designation. This overview includes any review meeting the definition of systematic, whether meta-analytic or qualitative, provided the intervention covered is performed in primary podiatric care or for which primary care podiatrists refer patients.

As explained in greater detail below, a catalog of reviews provides an immediately accessible overview of the state of the research literature by highlighting those research questions for which a quantity sufficient to warrant review effort, and presumably quality, of research has been published. Such a catalog also synthesizes a larger body of literature than otherwise would be feasible for any single review, while defining gaps in the knowledge base for a research agenda. Reviewers may find insufficient quantity or quality of published research to definitively answer their questions, but rigorous methods make even apparently negative findings valuable to understanding the knowledge base

Search strategy
TAP searched PubMed, the Cochrane library, and INAHTA databases using the terms "foot care", "systematic review", and "meta-analysis" for the years 1990 to 2009 to identify reviews published in English and covering research using adult human subjects.

RESULTS

The 37 reviews identified by TAP searches (exclusions noted above) are summarized in Table 1 and abstracted in detail in the Appendix table; in both cases listed in reverse chronological order. Reviews from the Cochrane Collaboration (www.cochrane.org) set the standard for methodological rigor and validity of results.

Table 1: Summary availability of systematic reviews for podiatry interventions
Full details in Appendix
Light shading indicates duplicate publications

Citation	Content/Intervention(s)
Diabetic foot/other wounds	
Bus (2008)	Footwear and offloading interventions
Dinh (2008)	Accuracy of physical examination and imaging tests for osteomyelitis underlying foot ulcers
Hinchliffe (2008)	Interventions to enhance healing
Crawford (2007)	Predicting foot ulcers in patients with diabetes
Kapoor (2007)	MRI for osteomyelitis
Shaw (2007)	Topical phenytoin
Vermeulen (Cochrane; 2007)	Topical silver for infected wounds of any etiology
ASERNIPS-S(2006)	Bioengineered skin substitutes for wound management
Nelson (2006)	Management of diabetic foot ulcer
Nelson (2006a)	
O'Meara (2006)	
O.Meara (2000)	
Majid (2000)	
Bergin (Cochrane; 2006)	Silver-based wound dressings and topical agents for DFUs
Cruciani (2005)	GCSF
Ho (CCOHTA; 2005)	Artificial skin grafts for chronic wounds
Adams (2003)	Collagen-based dressings for chronic wound management
MacIntosh (2003)	Guideline: prevention and management of foot problems in Type 2 diabetes
Pham (2003)	Vacuum-assisted closure for wound management
Sibbald (2003)	Cost-effectiveness of becaplermin
Sibbald (2003)	Cost-effectiveness: becaplermin for nonhealing neuropathic diabetic foot ulcers
Edwards (Cochrane; 2002)	Debridement
Steinberg (2002)	Living skin equivalent for diabetic foot ulcers
Kantor (2001)	Cost-effectiveness of treatment options for diabetic foot ulcers
Valk (Cochrane; 2001)	Patient education for preventing diabetic foot ulcer
Ubbink (Cochrane; 2001)	Topical negative pressure
Spencer (Cochrane; 2000)	Pressure relieving interventions
Total: 27 titles/23 independent reviews	**diabetic foot/other wounds**
Other review topics	
Hawke (Cochrane; 2008)	Custom orthoses for foot pain
Burns (Cochrane; 2007)	Prevention and treatment of pes cavus
Kapoor (2007)	MRI for diagnosing foot osteomyelitis
Kerkhoffs (Cochrane;2007)	Surgical Vs conservative treatment for acute injuries of lateral ligament complex
Keogh-Brown (2007)	Cost-effectiveness analysis of wart treatment
De Vries (2006)	Interventions for chronic ankle instability
Marsland (Cochrane; 2006)	Interventions for chronic palmoplantar pustulosis
Farrow (2005)	Interventions for foot disease in rheumatoid arthritis
Bachmann (2003)	Accuracy of Ottawa ankle rules for ruling out fractures of ankle and mid-foot
Crawford (Cochrane; 2003)	Interventions for plantar heel pain
Atkins (1999)	Treatments for painful heal

Citation	Content/Intervention(s)
Rounding (2003)	Surgical treatment of ingrowing toenails
McIntosh (NICE; 2003)	Prevention and management of foot ulcers in Type 2 diabetes
McLauchlan (2001)	Interventions for Achilles tendinitis
Total: 14	**Other review topics**
All reviews:37	**23(62%) for diabetic foot**

SUMMARY AND DISCUSSION

TAP did not identify review-worthy primary research on primary foot care as originally identified for this overview. Discussions with Podiatry Service agreed that a catalog of systematic reviews would meet their needs for an evaluation of the evidence base supporting routine interventions.

Some included reviews did ultimately address Podiatry's original toenail and callus issues, but only in context of control interventions for research designed to address other questions. As indicated above, diabetic foot and other wounds, major burdens for individuals and health care systems, are subjects for the majority of available reviews. Beyond burden of disease, the reviews cataloged here cover ranges of interventions and patient groups so wide that they defy summarization.

However, some common themes do emerge: the evidence base does not support firm conclusions on the efficacy of many podiatry interventions; and there are few reliably effective strategies for diabetic foot ulcers, although new technologies may hold promise. In this context, reviewers frequently fall back on "suggestions" from individual methodologically poor and short term studies.

Finally, while economic evaluations have been published, the questionable documentation of efficacy makes such analyses premature: those reported here meet minimal standards for inclusion, but rely on efficacy information from small numbers of uncritically selected primary studies.

More rigorously conducted and transparently reported research is urgently needed: TAP searched AHRQ's database (www.clinicaltrials.gov) of ongoing trials using "foot health" on November 10, 2009: of 179 ongoing studies, 16 will add additional if not definitive evidence to the review topics covered here. VHA's Podiatry Service may consider conducting or supporting its own research and TAP will continue to monitor the podiatry literature.

APPENDIX

Table 2: Abstracted details of systematic reviews

Asterisk indicates industry/for- profit support or employment of authors

Citation	Objective/interventions	Methods	Results/Conclusions
Diabetic foot and other problem wounds			
Bus (2008)	**What is evidence base for footwear and offloading interventions (casting, footwear, surgery, other) to prevent and heal DFUs?**	• Multiple databases, -2006 • Original research without date or language restrictions: RCTs; cohort; case-control, before-and-after; interrupted time series; cross-sectional; uncontrolled; or observational; excluded if one of reviewers was author • Quality assessment by Dutch Cochrane checklist	**<u>21 studies fully assessed</u>** **Prevention:** • No studies for primary prevention (first ulcer) with footwear but "several" for secondary prevention/recurrence; • One large RCT: NS difference in ulcer occurrence over several years with therapeutic Vs control shoes; • One small RCT: significant difference at 1 yr, therapeutic Vs subjects' own shoes; • Methodologic problems with both RCTs; • Other controlled studies: significant difference, clinical treatment + education+footwear Vs same intervention without footwear; therapeutic sandals better than leather board insole for recurrence prevention; • Surgery RCTs: ATL+ TCC better than TCC alone for forefoot plantar ulcer recurrence; excision + debridement + bone segment removal better than conservative treatment for preventing recurrence: • Other surgery controlled studies: positive effects for metatarso-phalangeal arthroplasty of great toe and metatarsal head resection for recurrence prevention. **Treatment:** • **Castings:** 3 RCTs: TCC and windowed TCC significantly better rates of healing than footwear interventions or removable walker, but RCTs may have been confounded by activity or compliance levels; • **Footwear:** controlled studies more often use footwear as control rather than active intervention; • Within design limitations: EVA boots, other types of shoes, or insoles may have roles in promoting healing; • **Surgical off loading:** one RCT found surgery + TCC better than TCC alone; another RCT with questionable statistical analyses found complex intervention (excision, debridement, bone removal, surgical closure) better than conservative treated alone; other studies found shorter healing time with surgery Vs TCC alone; • **Bed rest, crutches, canes, other offloading devices:** observational studies or underpowered controlled;

Citation	Objective/interventions	Methods	Results/Conclusions
			• **Plantar pressure reduction:** No controlled studies for casting device, footwear, or surgery. **Conclusions:***…" the evidence base to support the use of footwear and offloading in the prevention and treatment of DFUs is small and in some areas non-existent…the methodological quality is poor..best support from the evidence is for non-removable devices such as TCC and non-removable walkers in the treatment of neuropathic plantar DFUs. More high-quality controlled studies are urgently needed…"*
Dinh (2008)	**Meta-analysis of accuracy of diagnostic tests for osteomyelitis in DFUs**	**Multiple databases:** • 1966-2007; • English- language studies of diagnosis in adults; • Included: assessments of accuracy of clinical or imaging modalities against gold standard histology and/or culture of bone specimens.	**9/917 studies included:** • Variable study designs and quality; • Plain radiography: Se, 0.60; Sp, 0.91; • MRI: Se, 0.90, Sp, 0.79; • Bone scan; Se, 0.81; Sp, 0.28; • Leukocyte scan: Se, 0.74; Sp, 0.68; • Diagnostic ORs: clinical exam (49.45); radiograph (2.84); MRI (24.36); bone scan (2.1); leukocyte scan (10.07); **Conclusions:** *'The presence of exposed bone or a positive probe-to-bone test result is moderately predictive of osteomyelitis. MRI is the most accurate imaging test."*
Hinchliffe (2008)	**To identify interventions for chronic DFUs for which there is evidence of effectiveness**	**Multiple databases:** • 1966-2006; • Evaluations of interventions directed at adults with either type diabetes: RCTs; case-control; cohort; controlled before-and-after; interrupted time series; • No language restriction; • Quality assessment by Cochrane checklist.	**Sharp debridement and wound bed preparation with larvae:** • 3/626 studies included; • Surgical: one study (subgroup from RCT for different intervention):healing at 12 weeks more likely with vigorous debridement; • Larval (2 small studies): significant effect at 2 weeks; decreased healing time in elderly non-ambulant with peripheral arterial disease respectively. **Chemical (antiseptic or dressing) wound bed preparation:** • 11/98 studies included; • 1 study: no benefit to cadexomer iodine; • 1 RCT: zinc oxide tape decreased wound area at 5 weeks Vs hydrocolloid; • Alginate/collagen-alginate products: NS effects; • Hydrogels (3 studies): significant benefit Vs saline-moistened gauze; inadequate reporting to determine benefit in other 2 studies; • Carboxy-methyl cellulose hydrofiber dressing (1 small RCT): highly significant benefit Vs saline-moistened gauze at 6 weeks. **Resection of chronic wound:** • 4/879 studies included; • Excision of plantar ulcers with/without removal of underlying bone: reduced time to healing but no change in eventual healing rate overall; • One retrospective study (excision of 5th metatarsal head underlying ulcer): weak

Citation	Objective/interventions	Methods	Results/Conclusions
			effect Vs non-surgical management; similar design for excision under inter-phalangeal joint + arthroplasty: increased healing at 6 months and decreased recurrence; • Early infected soft tissue excision (hospitalization): decreased incidence of major amputation. **Hyperbaric oxygen:** • 65/114 studies included; • Topical HBO (2 studies): no apparent benefit at 1, 2, or 4 weeks; • Systemic HBO (4 RCTs):"some" evidence that systemic may reduce rate of major amputation; all studies small and with design limitations; **Reduction of tissue edema:** • 4/66 studies included, all in patients who had previously undergone surgery; • TNP: 2 very small RCTs: significant benefits in healing rate and time; • Single larger RCT: benefit to TNP (time and rate of healing); confounded by patients who healed after repeat surgery; **Conclusions:** *Of the 2251 papers identified, 60 were selected for grading following full text review. Some evidence was found to support hydrogels as desloughing agents and to suggest that systemic HBO may be effective. TNP may promote healing of post-operative wounds, and resection of neuropathic plantar ulcers may be beneficial. More information was needed to confirm the effectiveness and cost-effectiveness of these and other interventions. No data were found to justify the use of any pother topically applied product or dressing, including those with antiseptic properties. Further evidence to substantiate the effect of interventions designed to enhance the healing of chronic wounds is urgently needed. Until such evidence is available from robust trials, there is limited justification for the use of more expensive treatments and dressings."*
Shaw (2007)	**Effects of topical phenytoin on wound healing**	**Multiple databases:** • 1963-2005; • RCTs in humans reporting wound closure or healing over time; • Excluded: Non-English language or case series.	**14 RCTs:** • 12'/14 had quality score < 75% (low-to-moderate methodologic quality); • 2 scored > 75%; • Common failings: failure to describe randomization; lack of blinding; short-term outcomes only. **Conclusions:** *Overall, it would appear that studies investigating the effect of topical phenytoin on wound healing are of moderate methodological quality, and these suggest that there may be a positive effect on healing in a variety of wounds."*
Kapoor (2007)	**Diagnostic performance of**	**PubMed, Embase, and consultation**	**16 studies:**

Citation	Objective/interventions	Methods	Results/Conclusions
	MRI for osteomyelitis of the foot	**with experts:** • 1996-June 2006; • English-language studies of MRI in adults with foot suspected foot osteomyelitis; compared to biopsy/culture (gold standard); Vs plain radiographs or bone scanning (In or Tc); and 2x2 tables could be constructed; • Quality assessment by Cochrane criteria;	• Pooled DOR, 42.1 (CI, 14.8-119.9); • Sp at Se of 90% was 82.5%; • DOR did not vary among subsets of studies; • Where direct comparisons could be made: DOR for MRI consistently better than bone scanning (149.9 Vs 3.6 from 7 studies); plain radiograph (81.5 Vs 3.3 from 7 studies); and WBC scan (120.3 Vs 3.4 from 3 studies). **Conclusions:** *"MRI performs well in the diagnosis of osteomyelitis of the foot and ankle and can be used to rule in or out the diagnosis. Magnetic resonance imaging was markedly superior to that of technetium Tc 99m bone scanning, plain radiography, and white blood cell studies."*
Crawford (2007)	**Predictive value of diagnostic tests, physical signs and elements from history for DFUs**	**Multiple databases:** • Inception to 2005; • Case-control or cohort studies assessing predictive value of tests, signs and symptoms; • QUADAS checklist for quality asse4ssment; • Pooled estimates (WMDs) calculated	**16 studies:** • 5 case-control: used statistical adjustment for confounding; • 11 cohort: incidence of DFUs 8-17% with varying lengths of FU; • Tests and physical signs for peripheral neuropathy (biothesiometry, monoflaments, absent ankle reflexes) and those for excessive plantar pressure were all significantly associated with future DFUs; • However: paucity of evidence for predictive values of signs and symptoms. **Conclusions:** ***"****We found evidence to support the use of diagnostic tests and physical signs that detect peripheral neuropathy, the principle cause of diabetic foot ulceration. High vibration perception thresholds (VPTs) using a biothesiometer or tuning fork, high plantar pressure and 10g monofilaments appear reliable methods to identify those at risk for future ulceration. Absent ankle reflexes and limited joint motion at both the first metatarsal-phalangeal joint and the subtalar joint were also found to increase the risk of foot ulceration. These findings were evident across different study designs, polled. And unadjusted and adjusted estimates of effect. Established vascular disease, in the form of a history of previous ulceration, amputation or lower limb bypass procedures, was also consistently associated with risk of future ulceration.* *None of the published studies reported on the predictive value of signs associated with foot trauma, such as inappropriate footwear and* ***improperly cut toenails****.* *Evidence concerning the predictive value of 'contributory' factors in diabetic foot ulceration, such as some physical signs and elements from the patient's history, was less clear. For example HbA_{1c} and ankle branchial indices (ABI, ABPI, or AAI) produced inconsistent and contradictory findings. The length of time that a person had diabetes was marginally predictive in two cohort studies, although in five methodologically weaker case-control studies, the association was not statistically significant."*

Citation	Objective/interventions	Methods	Results/Conclusions
Vermeulen (Cochrane; 2007)	**Effects on wound healing (contaminated,/infected, acute or chronic):** • **Topical silver;** • **Silver dressings.**	**Multiple databases:** • - September 2006; • RCTs in adults with infected open wounds of any etiology (but not ostomies) and assessing dressings containing silver or with added silver; • Outcomes: objective measures of healing; adverse effects; antibiotic use; pain; patient satisfaction or QoL; LOS; costs.	**3 trials (847 subjects):** • Comparisons (one trial each): silver-containing foam (Contreet®) Vs hydrocellular foam (Allevyn®) in leg ulcers; silver-containing alginate (Silvercel®) Vs alginate alone (Algosteril®); silver-containing foam (Contreet®) Vs best local practice in chronic wounds; • Silver- containing foams did not significantly increase complete healing compared to standard foam or best practice up to 4 weeks of FU; but did reduce ulcer size and incidence of leakage; • Two trial assessed antibiotic use: NS differences; • Pain, satisfaction, LOS, and costs not assessed. **Conclusions:** *"Only three trials with a short follow-up duration were found. There is insufficient evidence to recommend the use of silver-containing dressings or topical agents for treatment of infected or contaminated chronic wounds."*
De Vries (Cochrane; 2006)	**Comparison of conservative and surgical treatments for chronic lateral ankle instability with or without (functional) mechanical laxity.**	**Multiple databases and contact with researchers:** • Inception – April 2006; • Randomized and quasi randomized trials; • Surgical interventions; rehabilitation programs after surgery; conservative interventions; • Languages other than English if translations could be obtained.	**7 trials:** • 0/7 methodologically flawless; • Only one trial described adequate randomization procedure; only two had moderate risk of bias; others high risk: pooling inappropriate; • Surgical interventions (4 studies): more complications after Chrisman-Snook procedure Vs anatomical reconstruction; variable findings from other studies; • Rehabilitation after surgery (2 studies): early functional mobilization led to earlier return to work and sports Vs immobilization; • Conservative intervention (1 study): better proprioception and functional outcome with bi-directional than with uni-directional pedal technique on cyclo-ergometer; **Conclusions:** *"In view of the low quality methodology of almost all the studies, this review does not provide sufficient evidence to support any specific surgical or conservative intervention for chronic ankle instability. However, after surgical reconstruction, early functional rehabilitation was shown to be superior to six weeks immobilization regarding time to return to work and sports."*
ASERNIP-S (2006)	**Safety and efficacy of bioengineered skin substitutes for management of wounds**	**Multiple databases:** • To April 2006; • RCTs in humans reporting wound closure; healing time; pain; exudates; cosmetics; exudate or complication	**23 RCTs:** • Most defined outcome as complete closure but secondary outcomes too inconsistent for meta-analysis; • venous leg ulcers (8 studies comparing Apligraf®, cryopreserved cultured alografts, Dermagraft®, EpiDex™, OASIS™, Pomogran™): comparable to standard treatment for healing time, closure, decreased ulcer area; no difference for pain, recurrence, or infection. • DFUs (6 studies): BSS appeared to offer advantage Vs controls; with wound healing time better with Apligraf®, Dermagraft®, GraftJacker®, Hyalograft™,

Citation	Objective/interventions	Methods	Results/Conclusions
			Laserskin™, OrCel™, and Promogran™; • other wounds (9):BSS NS healing Vs comparators, although pain might be better; • BSS with more favorable outcomes commonly had a dermal matrix component. **Conclusions:** *"The evidence base is rated as average, limited by generally small sample sizes, short follow-up periods, and lack of methodological rigor.* ***Safety:** The evidence suggests bioengineered skin substitutes for the management of venous leg ulcers, diabetic foot ulcers and other wounds are at least as safe as standard therapies for these indications."* ***Efficacy:** "The efficacy of bioengineered skin substitutes for the management of venous leg ulcers, diabetic foot ulcers and other wounds could not be determined based on the available evidence. Insufficient data on treatment durability were available."*
Bergin (Cochrane; 2006)	**Effects of silver-containing dressings and topical agents on infection rates and healing of DFUs.**	**Multiple databases , hand and internet searching:** • 1966-October 2004; • RCTs and controlled trials meeting requirements for allocation concealment and comparing silver-containing intervention to non-silver dressing, sham, or placebo; • Participants with Type 1 or 2 diabetes and foot ulcers; • Meta-analysis planned.	**No identified studies met inclusion criteria.** **Conclusions:** *"Despite the widespread use of dressings and topical agents containing silver for the treatment of diabetic foot ulcers. No randomized trials or controlled clinical trials exist that evaluate their clinical effectiveness. Trials are needed to determine clinical and cost-effectiveness."*
Nelson (2006)	**What are Se and Sp of different sampling techniques (wound swab, biopsy, lavage and/or curettage, near-patient testing) in identifying infection in DFU?**	• Multiple databases and hand searching, -2002; • Studies dealing with diagnosis, effectiveness, cost-effectiveness, economic or decision analytic modeling.	**Diagnosis:** 3 studies of diagnostic test performance in populations including people with DFUs; one for clinical assessment, one for punch biopsy Vs swab, one comparing quantitative and semi-quantitative swabs: • no evidence that single items on a clinical exam checklist were reliable for identifying infection in DFU; • wound swabs performed poorly against biopsy; • Semi-quantitative swab analysis may be useful alternative to quantitative. **Effectiveness:** 23 effectiveness studies, 2 cost-effectiveness of antimicrobials for DFU: • Majority of studies under-powered and too dissimilar to be pooled; • No strong evidence for any particular agent for prevention of amputation,

Citation	Objective/interventions	Methods	Results/Conclusions
			resolution of ulcer, or healing; • Topical pexiganan cream may be as effective as oral antibiotic treatment with ofloxacin for resolution of local infection;; • Ampicillin and sulbactam were less costly than imipenum and cilistatin; • GCSF was less costly than standard care; • cadexomer iodine dressings may be less costly than daily dressings. **Decision analysis (sampling and treating infected DFUs) based on series of reviews could not be completed as planned:** Insufficient information from reviews or interviews with experts to populate the model with transition probabilities; also insufficient information on probabilities of healing, amputation or death from intervention studies. **Implications for clinical care:** *"The available evidence was too weak to be able to draw reliable implications for practice. This means that, in terms of diagnosis, infection in DFUs cannot be reliably identified using clinical assessment. This also has implications for determining which patients need formal diagnostic testing for infection, whether empirical treatment with antibiotics (before the results of diagnostic tests are available) leads to better outcomes, and identifying the optimal methods of diagnostic testing. With respect to treatment, we do not know whether treatment with systemic or local antibiotics leads to better outcomes or whether any particular agent is more effective. Limited evidence suggests that both GCSF and cadexomer iodine may be less expensive than 'standard' care, that ampicillin/sulbactam may be less costly than impenum/silastatin and also that an unlicensed cream (pexiganan) may be as effective as oral ofloxacin."*
Ho (CCOHTA; 2005)	**Clinical efficacy, harm, and cost-effectiveness of artificial skin grafts for patients with disease-associated chronic skin wounds (DFUs, venous leg ulcers)**	Multiple databases, gray literature, and hand-searching: • - May 2004; • RCTs and economic evaluations reporting complete wound healing with or without artificial skin graft (Dermagraft, Apligraf; approved and available for use in N America, Europe, or Japan) over different time frames; • Trials assessed for quality with Jaddad scale; economic studies by Canadian criteria.	**17 RCTs:** • CWH higher for grafts than conventional treatment controls at 12 and 24 weeks but not 8 weeks regardless of ulcer type; • Apligraf produced greater gains than Dermagraft, but could be due to other factors (baseline risk or patient management). **6 economic studies:** • **Venous leg ulcers:** At 3 and 6 months: artificial skin associated with 22 and 60 ulcer-days averted at cost of C$14 and $1.04 per day respectively; • Over 1 year: moderate compression with Apligraf associated with 2.85 additional ulcer-free months and cost-savings of C$10,089. • **DFUs:** additional ulcer-free time over 1 year (2 months and 1.3 months); at additional cost if 7 pieces were used; 2 pieces were cost-saving. **Conclusions:** *"The results of clinical trials show that artificial skin grafts promote wound closure, resulting in more frequent and more rapid healing of diabetic foot*

Citation	Objective/interventions	Methods	Results/Conclusions
			ulcers, when compared with standard therapy. There is limited evidence of clinical efficacy of artificial skin grafts used for venous leg ulcers. In the short term, the use of artificial skin leads to increased costs. After one year, however, its clinical effects may result in net savings."
Cruciani (2005)	**Value of adjunctive GCSF for diabetic foot infections**	**Multiple databases:** • RCTs using GCSF as an adjunct to standard treatment for diabetic foot infections Vs standard therapy alone; • Jan 1990-July 2003; • Meta-analysis with heterogeneity and publication bias testing.	**5 RCTs (167 patients):** • Various GCSF preparations administered for 3-21 days; • Studies of satisfactory quality by Jaddad scale; • Meta-analysis: GCSF did not significantly effect resolution of infection or wound healing but was associated with reduced likelihood of surgical intervention(RR, 0.38; CI, 0.29-0.69), amputation (RR, 0.41; CI, 0.17-0.95); NNT = 8.6; • No evidence of heterogeneity or publication bias. **Conclusions:** *"Adjunctive GCSF does not appear to hasten the clinical resolution of diabetic foot infection or ulceration but is associated with a reduced rate of amputation and other surgical procedures. The small number of patients who need to be treated to gain this benefit suggests that using GCSF should be considered, especially in patients with limb-threatening infections."*
Adams (2003)	**Rapid review:** **Evidence supporting role of collagen-based products in wound care, specifically prevention of amputation?**	**Multiple databases, hand-searching and INAHTA query:** • English-language systematic reviews relevant to VHA needs; • Subsequently published review-eligible primary studies; • Through November 2002.	**Apligraf:** FDA-approved for: • Standard therapeutic compression for treatment of non-infected partial- or full-thickness skin ulcers due to venous insufficiency of greater than 1 month duration and which have not adequately responded to conventional ulcer therapy; • Standard diabetic ulcer care for treatment of full-thickness neuropathic diabetic foot ulcers of greater than 3 weeks duration which have not adequately responded to conventional ulcer therapy and which extended through the dermis but without tendon, muscle, capsule, or bone exposure. **Pomogran** FDA-indicated for: • Management of exuding wounds; • Including diabetic ulcers; venous ulcers; ulcers of mixed vascular etiology; full and partial thickness wounds at donor sites and other bleeding surface wounds; traumatic wounds healing by secondary intention; dehisced surgical wounds.
MacIntosh (2003)	**Guideline: prevention and management of foot problems in type 2 diabetes**	**Multiple database plus Internet and hand-searching:** • 1966-2003; • Studies addressing some aspect of screening, prevention, management, or education relating to foot care of people with diabetes;	**<u>Recommendations:</u>** **General management approach:** • Shared decision making; • Recall and annual review as part of ongoing care; • Annual review includes: foot exam for ulcer risk by trained provider; testing with 10g monofilament or vibration; palpation of foot pulses; inspection for deformity and footwear;

Citation	Objective/interventions	Methods	Results/Conclusions
		• Best evidence in each area selected: for interventions only systematic reviews of RCTs or RCTs were eligible; • Qualitative synthesis as meta-analysis generally not possible; • Evidence graded: Ia (meta-analysis of RCTs)-IV (consensus) and assessed for quality using detailed criteria (Appendices to guideline).	• Classify as: low current risk; increased risk; high risk; ulcerated. **Care of low current risk patients:** agreed management plan including education. **Increased risk patients:** • 3-6 monthly review by foot care team: inspection; determine need for vascular evaluation; evaluate footwear' enhance education. **High risk patients:** 1-3 monthly review: inspection; determine need for vascular evaluation; evaluate footwear; enhance education. **Patients with emergencies/ulcers (new ulceration, swelling, discoloration):** • Refer to multidisciplinary team within 24 hrs; • Minimum team standards: investigate and treat vascular deficiency; wound management (dressings, debridement); distribute plantar pressures (specialized footwear, orthotics, casts); optimal glucose and cardiovascular risk factor control. .
Pham (2003)	**Efficacy and safety of VAC for non-healing wounds**	**Multiple databases, hand searching:** • -2003; • RCTs of VAC in adults with any non-healing wounds;	**6 RCTs covering 4 indications:** • pressure sores (2 trials); DFUs (1); skin grafts (1); chronic and complex wounds (2); • 4 non-randomized CCTs: sternal wounds (3); skin grafts (1); • DFUs: VAC significantly decreased (28.4%) surface area Vs saline gauze (9.5%; p = 0.004). **Conclusions:** *Although most studies were probably too small to detect significant differences, some results did show VAC to result in better healing than standard methods, with few serious complications. More rigorous studies with larger sample sizes are required. With proper training to ensure appropriate and competent use, VAC is simple to use and appears to be a promising alternative for the management of various wound types."*
Sibbald (2003)	**What is the incremental cost-effectiveness (cost per ulcer day avoided) of adding bcaplermin to best clinical care on non-healing DFUs?**	**1-year decision model:** • results of best clinical care alone Vs with becaplermin from one 20-week RCT; • Best clinical care: treatment of ulcer cause and associations with debridement and daily dressing changes (hydrogel control) with weight offloading; • Adult patients with type 1 or 2	**Outcomes:** • Mean 26 fewer ulcer-days and small reduction in infected wounds with becaplermin (becaplermin efficacy 14% > placebo); • increased wound material interface costs and savings for local wound care; • Final incremental annual cost with becaplermin: $167/patient; • Sensitivity analyses varied 1-yr efficacy from 5% -25%> placebo; **Conclusions:** *" Over a 1-year period, the addition of up to 20 weeks of becaplermin to best clinical resulted in an important clinical benefit of 26 fewer ulcer-days per patient, along with an increase in total treatment cost. From the societal perspective*

Citation	Objective/interventions	Methods	Results/Conclusions
		diabetes. • Societal perspective; • Costs in 1998 Canadian$.	*recommended by most methodological guidelines, the incremental cost-effectiveness ratio is $6 per ulcer-day averted.* *Best clinical practice plus a trial of becaplermin gel implemented into a community setting for use in nonhealing neuropathic diabetic foot ulcers of the type in the clinical trial could offer a significant opportunity for improved patient outcomes…Results were sensitive to becaplermin cost, efficacy, and effect on infection and recurrence rates. The clinical benefits of becaplermin deserve further investigation to enhance cost-effectiveness information…"*
Edwards (Cochrane; 2002)	**Effectiveness of debridement for DFUs**	**Multiple databases and hand searching:** • -2007; • RCTs without language or publication restrictions	**6 RCTs:** • 3 for hydrogel debridement; one surgical, 2 compared hydrogels; one larval debridement; • Pooled results for hydrogels: more effective than gauze or standard care (RR, 1.84l CI, 1.3-2.61); • Surgical and larval debridement showed no significant benefit over standard care or hydrogels respectively in small trials. **Conclusions:** *"There is evidence to suggest that hydrogel increases the healing rate of diabetic foot ulcers compared with gauze dressings or standard care. More research is needed to evaluate the effects of widely used debridement methods and of debridement per se."*
*Steinberg (2002)	**Do incremental costs per ulcer-free month gained and amputation avoided with LSE Vs standard dressing fall within acceptable range for medical interventions?**	• Effectiveness data from one RCT (ADFUS); • Time: randomization to 6 months; • Direct costs as mean total costs from Medicare 2000 fee schedule in US$; • No indirect costs or perspective reported.	**112 LSE patients, 96 controls receiving standard dressings alone:** • NS baseline differences between groups; • Mean ulcer-free months higher for LSE than control (2.3 Vs 1.5; p = 0.010); • LSE group had fewer amputations/resections (5.4% Vs 12.5%; p = 0.085); • LSE group had fewer amputations/resections per patient (0.064 Vs 0.126; p = 0.073); • Amputations/patient without Charcot's disease: 0.06 Vs 0.178; p = 0.038; • Total mean costs/patient higher for LSE group: $7366 Vs $2020; p<0.001; • Incremental cost per ulcer-free month gained with LSE: $6683; per amputation/resection avoided: $86226; for those without Charcot, $41875; • Cost-effectiveness ratios sensitive to number of LSE applications. **Conclusions:** *The cost-effectiveness of LSE may improve in routine practice and among patients without Charcot's disease."…treatment of DFUs with LSE might be cost-effective especially if outcomes observed in the clinical trial are similar to those in routine clinical practice. As experience with LSE increases, it would be useful to perform further economic research exploring a longer time horizon and routine clinical practice outcomes associated with LSE."*
*Kantor (2001)	**Cost-effectiveness of common**	**Data sources:**	**Baseline effectiveness**(CI)**:**

Citation	Objective/interventions	Methods	Results/Conclusions
	treatments for DFUs: • **Standard care by GP or WCC** (covering wound with saline impregnated gauze; avoidance of weight bearing); • **Becaplermin** • **Platelet releasate.**	• Published RCTs and systematic reviews; • Database including 26,000 patients treated at Curative Health Services wound centers; • Costs in 1999$ from Medicare RBRVS.	• SC, 30.0% (26.6-35.1); • Becaplermin, 43.0% (37.3-48.7); • PR, 36.8%(35.4-38.2); • WCC, 35.6(34.,8-36.4). **Cost-effectiveness Vs SC:** • PR, 414.40; • Becaplermin, 36.59; • Incremental cost of increasing odds of healing by 1% over standard therapy: $414.40 (PR) and $36.59 (becaplermin). **Conclusions:** *"PR, becaplermin, and WCC all provided improved healing rates over standard care and becaplermin was less expensive and more effective than PR after 20 weeks of care."*
Valk (Cochrane; 2001)	**Effectiveness of patient education in preventing DFUs**	**Multiple databases:** • -September 2004 without language restrriction; • RCTs evaluating DFU prevention programs including education; • Critical appraisal by Cochrane criteria for RCTs and reporting incidence of DFUs; infection; amputation; ulcer recurrence; callus development; admissions for diabetic foot problems; foot care knowledge or behavior.	**9 RCTs included:** • 4 trials for brief education interventions, 2 with clinical endpoints: one reported reduction in ulcer incidence (OR, 0.29; CI, 0.13-0.59) and amputations (OR, 0.32; CI, 0.14-0.71) after 1 year; the second found NS difference at 7 years; • One trial showed improved foot care knowledge; another non-calcaneal callus reduction. • Conflicting results for patient-tailored education in addition to usual care; • RCT quality was poor: internal validity score 2-5 out of possible 10. **Conclusions:** *"RCTs evaluating education for people with diabetes, aimed at preventing foot ulceration, are mostly of poor methodological quality. Weak evidence suggests that patient education may reduce foot ulceration and amputations, especially in high-risk patient. Foot care knowledge and behavior of patients seems positively influenced by education in the short term."*
Ubbink (Cochrane; 2001)	**Effectiveness of topical negative pressure for wound healing**	**Multiple databases, hand searching:** • -2007 without language restrictions; • RCTs evaluating any form of TNP in people with chronic wounds and reporting an objective measure of wound healing; • Quality assessment by Cochrane criteria.	**7 trials (205 subjects):** • 5 different comparisons: Vs 0.9%saline- or Ringers-soaked gauze; hydrocolloid gel plus gauze; treatment package) topical papain-urea, cadexmer iodine or hydro-colliod, hydrogels, alginate, foam); • TNP did not increase healing rate Vs comparators; • Secondary outcomes (infection, QoL, edema, bacterial load, hospitalization) not reported. **Conclusions:***" Trials comparing TNP with alternative treatments for chronic wounds have methodological flaws and do not demonstrate a beneficial effect for TNP. However, more better quality research is needed."*

Citation	Objective/interventions	Methods	Results/Conclusions
Majid (2000): overlaps with Nelson (2006 and 2006a) O'Meara (2006 and 2000)	• Clinical and cost-effectiveness of interventions to prevent and treat diabetic foot ulcers? • Significant gaps in research evidence? • Research agenda for NHS?	• Multiple databases and hand-searching to end of 1998; • RCTs and economic evaluations without language or date restrictions; • Quality assessment: allocation concealment; sample size calculation; baseline comparability of groups; explicit inclusion/exclusion criteria; adequate FU description of withdrawals; ITT analysis.	**Prevention:** • One large trial (screening and foot protection): significantly fewer major amputations in intervention group; • 2 small custom footwear trials: significant benefit to callus eradication over podiatry (OR, 18.84; CI, 6.02-58.96); and significant reduction in ulcer recurrence with therapeutic shoes plus custom insoles (OR, 0.29; CI, 0.11-0.74); • One trial of outpatient podiatric care: significantly greater callus reduction with intervention; • One trial of compression hosiery: lower but NS ulcer incidence; • 1/5 trials evaluation educational interventions for ulcer prevention: significant benefit to brief simple education package (OR, 3.31; CI, 0.15-0.63). **Treatment:** • One trial of TCC: significantly more ulcers healed with TCC than standard treatment (OR, 11.59; CI, 3.27-41.09); • Two trials compared skin replacement dressings: pooled data indicated NS difference (OR, 1.47; CI, 0.88-2.45); • One trial of systemic HBO: significant reduction in amputations; • Topical HBO: NS difference; • 2 trials of topical ketanserin: significantly increased rate of ulcer healing but no effect with oral ketanserin; • Preliminary studies on iloprost and prostaglandin E_1: suggest possible benefits; • 5 trials of topical growth factors: pooled results on PDWHF/CT-102 make intervention more effective in healing ulcers than saline; • One multicenter trial: PDGF more effective than placebo (R, 2.67; CI, 1/27-5.65); • Growth factor studies were of relatively good quality but too small for definitive conclusions; • 9 trials on non-drug interventions and topical applications; all too small for definitive conclusions; • Neither of two trials for debriding agents (zinc oxide tape or cadexomer iodine) demonstrated impact on ulcer healing; • 2 antibiotic trials (one Vs placebo: NS differences. **Conclusions:** *"Much uncertainty remains over the most effective and cost-effective interventions for the prevention and treatment of diabetic foot ulcers. However, certain interventions (e.g. growth factors, skin replacements) show promise but need further and more rigorous evaluation. Future studies should take account of those interventions that have shown promise in these 'pilot' studies, and build on what has been learned, by choosing appropriate comparison treatments for trials., ensuring an adequate sample size and avoiding the shortcomings of the existing studies. In addition, there is little evidence of the longer term effectiveness of these treatments, as the majority of studies did not incorporate a long follow-up. The role of weight-*

Citation	Objective/interventions	Methods	Results/Conclusions
			bearing as part of the overall treatment needs to be clarified through further investigation. Researchers may wish to consider the development of a condition-specific outcome measure for diabetic foot studies, and it is clear that researchers need to be mindful of the need for unbiased, objective assessment of ulcer healing in future trials. In the absence of any clear evidence, this review strongly suggests that more good quality RCTs, alongside economic evaluations, are needed to determine the relative clinical- and cost-effectiveness of these interventions."
O'Meara (2000)	**Duplicates Nelson (2006, 2006a) and O'Meara (2006), above**		
Spencer (Cochrane; 2000)	**Effectiveness of pressure relieving interventions for prevention and treatment of DFUs**	**Multiple databases, hand searching:** • -1999 without language restriction; • RCTs evaluating any pressure relieving intervention to prevent or treat DFUs and reporting complete healing.	**4 RCTs:** • In-shoe orthotics appear to be of benefit in prevention although relative merits of different types unclear; • Other pressure relieving interventions (running shoes, removable casts, foam inlays) have not been evaluated; • 1 trial of TCC suggested effectiveness in treatment although evidence was limited. **Conclusions:** ***Prevention:*** *"There is limited evidence of the effectiveness of orthotic interventions over removal of callus. There is some evidence evaluating the relative effectiveness of two types of orthotic devices.* ***Treatment:*** *"There is very limited evidence of the effectiveness of total contact casts in the treatment of diabetic foot ulcers.* *Overall there is a need to measure the effectiveness of pressure relieving interventions for the prevention and treatment of diabetic foot ulcers as there is a small amount of poor quality research in this area."*
Other review topics			
Burns (Cochrane; 2007)	**Effects of interventions for prevention and treatment of pes cavus.**	**Multiple databases:** • 1966-April 2007; • Randomized and quasi-randomized trials in any language and reporting quantifiable measure of pain or change in level of pain at 3 months after intervention • Cochrane grading system for quality assessment; • Any intervention aimed at	**One trial for custom orthoses:** • Significant reduction in foot pain (WMD, 10.90; CI, 3.210-18.95); significant improvement in function for custom Vs sham orthoses; • 2 additional cross-over trials (OTC orthoses and footwear, both assessing secondary outcomes < 3 months) also included. **Conclusions:** *"In one randomized controlled trial, custom-made foot orthoses were significantly more beneficial than sham orthoses for treating chronic musculoskeletal foot pain associated with pes cavus in a variety of clinical populations. There is no evidence for any other type of intervention for the treatment of foot pain in people with a cavus foot type."*

Citation	Objective/interventions	Methods	Results/Conclusions
		prevention or treatment: appliances, physical therapies, medications; surgery; • Studies with different FU periods combined if assumption of stead rate of change justified.	
Kapoor (2007)			
Kerkhoffs (Cochrane; 2007)	**Relative effectiveness of treatments for ankle sprains:** • **Surgical;** • **Conservative (immobilization with cast or splint);** • **Functional (early mobilization with functional support/brace).**	**Multiple databases:** • 1966-Jan 2006; • Randomized or quasi-randomized trials comparing surgical with other interventions in adults; • Meta-analyses where appropriate; • Sensitivity analyses.	**20 trials (2562 mostly young active adult males):** • All trials had methodologic weaknesses with allocation concealment reported in only one; • Data appropriate for pooling available only in 12 trials and< 60% of participants; • Statistically significant differences in favor of surgery for 4 outcomes: non-return to pre-injury level of sports; sprain recurrence; long-term pain; subjective or functional instability; but not robust and heterogeneous; • Functional implications for higher incidence of objective instability in conservatively treated sprains uncertain: limited evidence for longer recovery; higher incidence of stiffness/impaired mobility; and complications with surgery. **Conclusions:** *"There is insufficient evidence available from randomized controlled trials to determine the relative effectiveness of surgical and conservative treatment for acute injuries of the lateral ligament complex of the ankle. High quality randomized controlled trials of primary surgical repair versus best available conservative treatment for well-defined injuries are required."*
Keogh-Brown (2007)	**Cost-effectiveness of wart treatment:** **Each treatment compared by Markov model with spontaneous resolution/ no treatment + plus basic GP advice** • OTC salicylic acid; • Salicylic acid prescribed by GP; • Cryotherapy by GP; • Duct tape.	• Efficacy based on Cochrane review (Gibbs; 2006); • Sensitivity analysis varied probabilities of cure	**No treatment:** 46% of patients' warts resolve by 18 weeks at no cost. **Advice only from GP:** same cure rate but costs £26.90 (GP consultation and travel) **3 sessions of cryotherapy; OTC cryotherapy; cryotherapy by nurse:** same cure rates but different costs: • Duct tape was most cost-effective but published evidence is lacking; • Salicylic acid most cost-effective OTC treatment; • GP cryotherapy less cost-effective than GP salicylic acid or nurse cryotherapy. **Conclusions:** *"Duct tape could be adopted as the primary therapy for cutaneous warts if its effectiveness is verified by further rigorous trials. Nurse-administered cryotherapy is likely to be more cost-effective than GP-administered cryotherapy."*
De Vries (2006)			
Marsland (Cochrane; 2006)	**Effectiveness of treatments for chronic palmo-plantar**	**Multiple databases:** • -March 2005 without language	**2 3 trials (724 subjects):** • Evidence supports systemic retinoids (improvement rate difference, 44^%; CI,

Citation	Objective/interventions	Methods	Results/Conclusions
	pustulosis	restriction; • RCTs in which PPP patients diagnosed by dermatologist receive one or more interventions	26-62); • Combination of PUVA + retinoids better than either; • Topical steroid under hydrocolloid occlusion is beneficial; • Low dose cyclosporine, tetracycline antibiotics and Ganz ray therapy may be useful; • Colchicine has high rate of adverse effects and uncertain effectiveness; • Topical PUVA: rate difference, 0.00; CI, -0.0-4 - 0.04; • No evidence suggests effectiveness for short-term treatment with hydroxyurea. **Conclusions:** *"Many different interventions were reported to produce "improvement" in PPP. There is, however, no standardized method for assessing response to treatment, ad reductions in pustule count or other empirical semi-quantitative scoring systems may be of little relevance to the patient. The ideal treatment for PPP remains elusive and the standards of study design and reporting need to be improved to inform patients and those treating them of the relative merits of the many treatments available."*
Farrow (2005)	**What is the evidence base for efficacy and harm of interventions for foot disease in RA?**	**Multiple databases:** • 1968-2003; • English-language RCTs, CCTs, cohort, or large retrospective observational studies (> 50 patients); • Quality assessment by Jadad scale;	**33/891 included:** • 5 RCTS (orthoses); 1 CCT; 25 cohort; 12 retrospective >50 (all for surgery); • 1 RCT (2 publications) was high quality: NS difference in pain or function for functional shoe insert with thin insole over 3 yrs; • Functional custom semi-rigid orthoses and extra-depth shoes were effective in single RCTs of variable quality; • No controlled trials for surgery; **Conclusions:** *"RCT evidence shows that orthoses and special shoes are likely to be beneficial in patients with RA. The only evidence of benefit from surgery comes from observational studies, because no RCTs have been conducted. Further RCT evidence is needed, although well-designed observational studies may be helpful."*
Bachmann (2003)	**Accuracy of Ottawa ankle rules for exclusion of ankle and mid-foot fractures**	**Multiple databases:** • 1990-2002; • " assessments of Ottawa ankle rules" without language restriction and allowing construction or 2x32 table	**32 studies; 27 reporting on 15,581 patients used for meta-analysis;** • Pooled negative likelihood ratios: ankle (0.08; CI, 0.03-0.18); mid-foot (0.08; CI, 0.03-0.18); • Applying likelihood ratios to 15% fracture prevalence: <1.4% probability of fracture in both subgroups. **Conclusions:** *" Evidence supports the Ottawa ankle rules as an instrument to exclude fractures of the ankle and mid-foot. This instrument has a sensitivity of about 100% and a modest specificity. Its use should reduce the number of unnecessary radiographs by 30-40%."*
Crawford (Cochrane;	**Effectiveness of treatments for**	**Multiple databases, hand-**	**19 RCTs (1626 subjects):**

Citation	Objective/interventions	Methods	Results/Conclusions
2003)	**plantar heal pain**	**searching, consultation with experts:** • Randomized and quasi-randomized trials in adults without language restriction; • 1988-2002; • Outcomes: pain; tenderness; disability; QoL.	• Trial quality generally poor, precluding pooling of data; • All trials measured heal pain; • Intervention Vs placebo/dummy or no treatment (7 trials): limited evidence for topical corticosteroid administered by iontophoresis (electric current) and injected corticosteroid in reducing/temporary relief of pain; • Conflicting evidence for low energy extracorporeal shock wave therapy in reducing night pain, resting pain, and pressure pain at 6-12 weeks; evidence in longer term or chronic pain equivocal; • Limited evidence for dorsi-flexion night splints in reducing pain; • No evidence for: therapeutic ultrasound; low-intensity lasers; electron generating device; or magnetic foil insoles. **Conclusions: "***Although there is limited evidence for the effectiveness of local corticosteroid therapy, the effectiveness of other frequently employed treatments in altering the clinical course of plantar heel pain has nit been established in randomized controlled trials."*
Pham (2003)			
Rounding (Cochrane; 2003)	**What is the effectiveness of surgical methods for treating in-growing nails?**	**Multiple databases plus hand-searching:** • Randomized or quasi-randomized trials comparing one form of surgery to another or to other treatments; • Reporting regrowth/relief of symptoms (primary outcomes); healing time, infection, post-operative pain; • at least 6 months FU for determination of cure; • Quality assessment: allocation concealment; ITT analysis; baseline comparability of groups; completeness of FU.	**9 included studies:** blinding not possible due to nature of procedure **Avulsion with phenol Vs surgical excision:** Phenol plus simple avulsion more effective than more invasive excisions in preventing symptom recurrence at 6 months (OR, 0.44; CI, 0.24-0.80). **Avulsion with phenol Vs without phenol:** Addition of phenol when performing a total or partial nail avulsion reduces recurrence rate (OR, 0.07; CI, 0.04-0.12), which is offset by increased post-operative infection rate (OR, 5.69; CI, 1.93-16.77). **Conclusions:** *"The evidence suggests that simple nail avulsion combined with use if phenol, compared to surgical excision techniques without use of phenol, is more effective at preventing symptomatic recurrence of ingrowing toenails.* *The addition of phenol when simple excision is performed dramatically decreases symptomatic recurrence, but at the cost of increased post-operative infection."*
McLaughlan (2001)	**Effectiveness of treatments for Achilles tendinitis**	**Multiple databases:** • -December 2000; • Randomized or quasi-randomized trials in adults; • Excluded: pathological tendinitis; comparisons of different NSAIDs or NSAID doses.	**9 trials (697 patients):** • Methodologic quality adequate for most but assessment of outcome incomplete and short-term; • Weak but not robust evidence(3 trials) for modest benefit to NSAIDs in alleviation of acute symptoms; • Weak evidence for no difference Vs no treatment: low-dose heparin; heel pads topical laser; and peri-tendon steroid injection; but not fully evaluable from

Citation	Objective/interventions	Methods	Results/Conclusions
			reports; • Experimental calf-derived deproteinized hemodialysate promising but only one small trial possibly confounded by severity of disease. **Conclusions:** *"There is insufficient evidence from randomized controlled trials to determine which method of treatment is the most appropriate for the treatment of acute or chronic Achilles tendinitis. Further research is warranted."*

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TECHNOLOGY ASSESSMENT PROGRAM

Mission Statement

To enhance the health of veterans and the nation by providing and fostering technology assessment for evidence-based health care

Values

Integrity and pride in the work that we do

Quality products that are clinically valid and methodologically transparent

Objectivity in evaluating and presenting research evidence

Commitment to continuous quality improvement and to the guiding principles of evidence based practices

Flexibility in responding to changes in VA and the larger healthcare environment

Innovation in designing products and their dissemination to best meet VA's needs

Accessibility of products and services